CONCLUSION

Patient: 779
Gender: Male
Date of Birth:
Material Type: DNA
Date of pickup: 10/01/2015
Diagnosis: Congenital autosomal recessive cataract

Likely pathogenic mutations that are a possible cause of the disease

Position (hg19)	Genotype	Gene	Position in mDNA	Amino acid replacement	Exon	Transcript	Allele frequency*	Reading depth
chr3:46009205G>A	A/A	FYCO1	c.1621C>T	p.Gln541Ter	8	NM_024513.4	N/A	303x

* - Allele frequencies are based on the Exome Aggregation Consortium database (sample up to 60702 people). N/A = no data (not described)

INTERPRETATION

Patient No. 779 was searched for pathogenic mutations associated with congenital autosomal recessive cataract, as well as other hereditary diseases with similar phenotypic manifestations. A previously undescribed homozygous mutation in exon 8 of the FYCO1 gene (chr3: 46009205G> A) was revealed, leading to the appearance of a premature translation termination site in the 541 codon (p.Gln541Ter, NM_024513.3). Homozygous mutations in the FYCO1 gene are described in patients with autosomal recessive cataract type 18 (OMIM: 610019). The mutation was not registered in the control samples "1000 genomes", ESP6500 and ExAC. Since the mutation disrupts the synthesis of a full-sized protein, it should be regarded as probably pathogenic. The result requires careful comparison with clinical signs. No other significant changes matching the search criteria were found.

RESEARCH DESCRIPTION

The patient’s DNA analysis was carried out on a new generation sequencer Illumina NextSeq 500 using the pair-end reading method (2x151 bp) with an average coverage of at least 70-100x. For sample preparation, we used the technique of selective capture of DNA regions belonging to the coding regions of human genes.

The sequencing data were processed using an automated algorithm, including alignment of reads to the reference sequence of the human genome (hg19), postprocessing of alignment, identification of options and filtering of options by quality, as well as annotation of the identified options for all known transcripts of each gene from the RefSeq database using a number of methods predictions of pathogenicity of substitutions (SIFT, PolyPhen2-HDIV, PolyPhen2-HVAR, MutationTaster, LRT), as well as methods for calculating the evolutionary conservatism of positions (PhyloP, PhastCons).

To assess the population frequencies of the identified variants, we used samples of the 1000 Genomes, ESP6500, and Exome Aggregation Consortium projects. To assess the clinical relevance of the identified options, the OMIM database, specialized databases for individual diseases (if any), and literature data were used. In conclusion, only options that are possible related

to the clinical manifestations of the patient are included. Polymorphisms classified according to various criteria as neutral are not included in the conclusion. Limitations of the method: the method does not allow detection of insertions and deletions longer than 10 bp, mutations in intron regions (except for canonical splicing sites), variations in the length of repeats (including expansion of triplets), as well as mutations in genes in which the paralog (pseudogen) is close in sequence to the genome. The method is not intended to determine the phase of pairs of heterozygous mutations, as well as to assess the level of methylation, identify chromosomal rearrangements, polyploidy, identify mutations in a state of mosaicism.

QUALITY INFORMATION

Total reads	68118091	**Total options revealed**	188338
Read length	2x151 bp	**Options after filtration according to the basic criteria of pathogenicity and assessment by clinical criteria**	1
Read nucleotides	18.30 billion		
Average coverage	162.7x		

LINKS TO USED DATABASES AND LITERATURE

1. http://www.ncbi.nlm.nih.gov/clinvar/
2. http://www.omim.org/
3. http://www.ncbi.nlm.nih.gov/snp/
4. http://evs.gs.washington.edu/EVS/
5. http://exac.broadinstitute.org/